

Viral Hepatitis

Epidemiology

Diagnosis

Prevention

Revised Nov 99

Objectives

Recognize Signs and Symptoms

Interpret Laboratory Results

Understand Hepatitis Epidemiology

Implement Appropriate Preventive
Measures

Fill Out the Medical Event Report

References

- BUMEDINST 6230.15, Immunizations and Chemoprophylaxis, Nov 95
- BUMED Notice 6230, Imm. Req. & Rec, Apr 98
- BUMEDINST 6220.12A, MERs, Oct 98
- Control of Communicable Diseases Manual
- CDC Hepatitis Resource Center

Overview

Symptoms

Hepatitis Viruses A-E

Serologic diagnosis

Epidemiology

Prevention

Reporting requirements

Cases for Discussion

Terms & Definitions

Hepatitis

Inflammation of the liver

Enterovirus

A virus which infects the gastrointestinal system

Antibody

A protein in the blood generated in response to foreign proteins or polysaccharides. Sometimes antibodies provide protection from infection.

Terms & Definitions

Antigen

Any substance that stimulates production of an antibody

Viral antigen

Any part of a virus that stimulates an antibody response

Viral Hepatitis

A systemic infection which causes inflammation of the liver

Currently 5 recognized types:
A, B, C, D, E

All 5 viruses cause similar illness, but have distinct antigenic properties

Viruses Associated with Acute Hepatitis

Common in U.S.*

- Cytomegalovirus
- Epstein-Barr
- Herpes simplex
- Varicella zoster
- Measles
- Rubella
- Coxsackie

Exotic**

- Yellow fever
- Argentinean hemorrhagic fever
- Bolivian hemorrhagic fever
- Lassa fever
- Rift Valley fever
- Marburg
- Ebola

* Each causes less than 1% of acute hepatitis.
seen in the U.S.

** Not
8

Acute Hepatitis:

Common Symptoms *Uncommon*

- Malaise 76-94%
- Anorexia 94-96%
- Dark urine 65-94%
- Nausea 61-81%
- Abdominal pain 26-68%
- Scleral icterus 48%
- Vomiting 20-37%
- Asymptomatic
- Respiratory symptoms
- Headache
- Fever
- Muscle pain
- Rash
- Joint pain
- Itching

Acute Hepatitis: Signs

Jaundice	70-90%
Hepatomegaly	14-69%
Tender liver	20-86%
Rash	40%
Splenomegaly	3-21%
Fever	1-8%
High LFTs	100%

Hepatitis A

“infectious hepatitis, epidemic hepatitis”

Caused by a small RNA enterovirus of the picornavirus family

Causes about 25-50% of acute hepatitis in the U.S. and other developed countries

High prevalence in west Pacific, southeast Asia, Africa, and other developing countries

Hepatitis A: Clinical Aspects

Onset: usually abrupt

Duration

Mild lasting 1-2 weeks

Severe lasting months

Rarely fatal

80% of children asymptomatic

Adults are usually symptomatic and jaundiced. Nausea, vomiting, & fever are common.



Hepatitis A: Transmission

Person to person

Poor personal hygiene

Poor sanitation

Intimate contact

Contaminated food or water

Not transmitted by sharing
utensils, cigarettes, kissing

Hepatitis A

Incubation

15-55 days, average 28 days

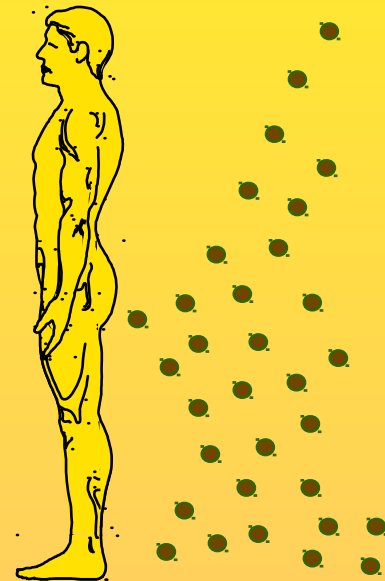
Greatest infectivity

2 wks before jaundice appears

Fecal viral shedding

Greatest during late
incubation and prodrome

Diminishes rapidly after
jaundice occurs



Hepatitis A: Diagnosis

1. Acute symptoms
2. Elevated LFTs
3. IgM anti-HAV (antibody to hepatitis A virus) appears early and remains only 4-6 months. It confirms diagnosis of *acute* hepatitis A.

Total anti-HAV (combination of IgM & IgG) is detectable early & persists lifelong.

It does not confirm *acute* hepatitis A.

(About 1/3 of U.S. population has IgG anti-HAV)

Hepatitis A: Prevention

- Sanitation

- Education

 - Safe food, water, and ice

 - Good personal hygiene

- Vaccination

- Standard immune globulin (IG)

Hepatitis A Vaccine

Two brands available - interchangeable

Adult dose

- 1 ml, given at least 2 weeks before travel

- Single 1 ml booster, 6-12 months later

Required for all active duty and Select Reserve

Recommended for family members, ages 2 and older, and DoD civilian personnel who travel or live in endemic countries.

Standard immune globulin (IG)

A sterile solution of antibodies prepared from human plasma

85% effective when given IM before exposure or within 2 weeks after exposure

Vaccination 2 weeks prior eliminates need

Limited availability

DoD stock - use solely for emergency

Hepatitis A & Food Workers

High potential for outbreaks

Verify diagnosis

Evaluate food related duties, types of food, preparation methods

Some food related work is low risk

Wearing gloves reduces risk

Consider IG prophylaxis

Fellow food handlers are more at risk than diners

Hepatitis A: Review

Acute onset after 28 days
incubation

Spread by fecal contamination

Good hygiene prevents spread

Vaccine preventable

IG provides protection, but only if
given within 2 weeks of exposure

Hepatitis B

“serum hepatitis, post-transfusion hepatitis”

Double shelled DNA hepadnavirus

Onset insidious

(subtle and treacherous)

Symptoms more severe

Arthralgias, rash, nausea & vomiting

Often hospitalized

One in 200 die from acute disease

Chronic liver disease kills ten times as many

Transmission

Virus present in blood, semen, saliva

Transmitted across skin or mucous membranes

Percutaneous

Contaminated needles (Tattoos, piercing, drugs, etc)

Blood transfusion

Perinatal

Hepatitis B: Transmission

Per mucosal

Sexual contact

Continuous close contact

Household contacts

Institutions for the mentally
retarded

Patients and staff

Hepatitis B

Incubation period: 45-160 days, average 120

Infectious period varies

- 30 days after exposure

- 6 months after onset

- Chronic carriers remain infectious > 6 months

Frequency

- 25-50% of new acute hepatitis cases in U.S.

- 0.3 % U.S. first time donors are HBsAg+

- 10-20 % of institutionalized retarded persons

- 13% of immigrants born in endemic countries

Hepatitis B: Diagnosis

1. Symptoms
2. Elevated LFTs
3. Confirmed by serology
 - IgM anti-HBc (IgM core antibody)
 - HBsAg (surface antigen)
 - HBsAb/anti-HBs (antibody to surface antigen)
 - HBcAb/anti-HBc (antibody to core antigen)
 - HBeAg (E antigen)
 - HBeAb/anti-HBe (antibody to E antigen)

Hepatitis B Virus

Shell with surface antigen

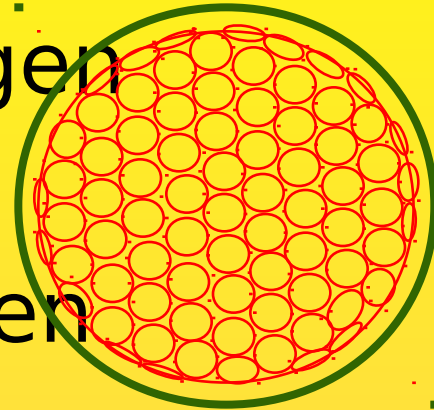
Inside the shell

Core with core antigen

Inside the core

DNA

E antigen



Hepatitis B Diagnosis

Serology

IgM anti-HBc (core antibody)

- Appears early
- Persists for 6 months

HBsAg (surface antigen)

- Detectable 30-60 days after exposure
- May indicate chronic carrier status

HBsAb (antibody to surface antigen)

- Develops after resolved infection
- Indicates long term immunity

Serology

Anti-HBc/HBcAb (antibody to core antigen)

- Develops in all HBV infections

HBeAg (E antigen)

- Indicates HBV replication
- Correlates with high infectivity
- Present in acute or chronic infection

Anti-HBe (antibody to E antigen)

- Develops in most HBV infections
- Correlates with lower infectivity

Chronic Carrier State

2 positive HBsAg tests 6 months
apart

or

Positive HBsAg with
Negative anti-HBc IgM

Chronic Carrier State

90% of infants	}	Risk of chronic infection is lower after acute illness
30% of 5 year olds		
6% of adults		

Prolonged infection can occur without signs or symptoms of acute or chronic illness

Chronic Carrier State

10% / yr lose HBeAg - become noninfectious

1-2% / yr lose HBsAg - become non-carriers

25 % will develop chronic active disease

20% will develop cirrhosis

5% will develop hepatocellular cancer

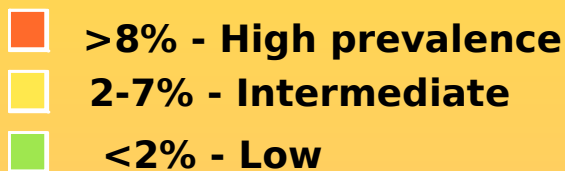
HBV causes 85% of primary liver cancer
worldwide

Hepatitis B Complications

Hepatitis B

Major cause of acute & chronic hepatitis,
cirrhosis, and hepatocellular cancer

Worldwide



Hepatitis B is the second
most preventable cause of
cancer



Hepatitis B is an STD

Many prostitutes
in the Philippines, Thailand,
and developing countries
are hepatitis B carriers

Sexual activity is #1 risk factor in
U.S.

Chronic Carriers

Active duty Navy or Marine Corps personnel who become HBV carriers, but who do not have evidence of chronic persistent or recurrent active hepatitis must not be restricted from full duty.

Chronic Carriers

Asymptomatic HBV carriers need annual medical evaluation.

Medical Department personnel who are chronic carriers are not restricted.

HBV carriers with persistent symptoms or elevated LFTs, who are retained on active duty, need periodic evaluation.

Hepatitis B Prevention

Education

Needles, sex, universal precautions

Vaccine

Pre-exposure, active immunity

HBIG

Post-exposure,
passive immunity



Hepatitis B Vaccine

Recombivax-HE or Engerix-B
Interchangeable - 3 dose series
Day zero, day 30, 6 months

1/2 dose (0.5 ml) OK for under age 30

DO NOT RESTART SERIES

Hepatitis B Vaccine

Required

Health care workers

Hospital Corps & dental techs

New Medical Department officers

Patients with STDs

Public safety workers

Correctional facility workers

Compliance with OSHA regulations

Hepatitis B Vaccine

Pre-vaccination screening

Not recommended

Post-vaccination testing

Identify non-responders in high risk jobs

Non-responders receive one additional 3-dose series of hepatitis B vaccine, but not a third

HBIG (Hepatitis B immune globulin)

Post-exposure prophylaxis

Passive immunity

High concentration of anti-HBs

Indications

Perinatal exposure to HBsAg+ mother

Percutaneous or permucosal exposure to HBsAg+ blood

Sexual exposure to HBsAg+ person

Also need 3 dose vaccine series

Hepatitis B: Review

Serious health threat

Transmitted via blood and sex

Lots of antigens and antibodies

HBsAg: person has infection

HBsAb: person has immunity

Hepatitis B vaccine prevents

Hepatitis C

“transfusion related non-A, non-B hepatitis”

Caused by RNA flavivirus

Accounts for 25% acute hepatitis in U.S.

Transmission similar to hepatitis B

Parenteral > sexual > perinatal

Range of symptoms and sequelae similar to hepatitis B

Hepatitis C

Occurs worldwide

Responsible for 90% of post-transfusion hepatitis in U.S. prior to 1990

1970s 7-12% post-transfusion risk

1980s 1-4% risk (ALT screening 1986)

1990s < 1% risk in (screening started 1990)

Most cases now are community acquired

Hepatitis C: Clinical Aspects

Incubation period Average 6-7 wks
Range 2-26 wks

Clinical illness / jaundice occurs in 20-40%

Fulminant hepatitis & death occurs 1-2%

Chronic infection and liver damage occurs
in most cases, but is slow to develop

Hepatitis C: Complications

Chronic carriers

- 75-85% develop persistent infection

- 70% develop chronic liver disease

- 20-30% progress to cirrhosis

- Can also lead to liver cancer

- Alcohol use worsens chronic disease

Hepatitis C Diagnosis

1. Symptoms
2. Elevated LFTs
3. Confirmed by serology

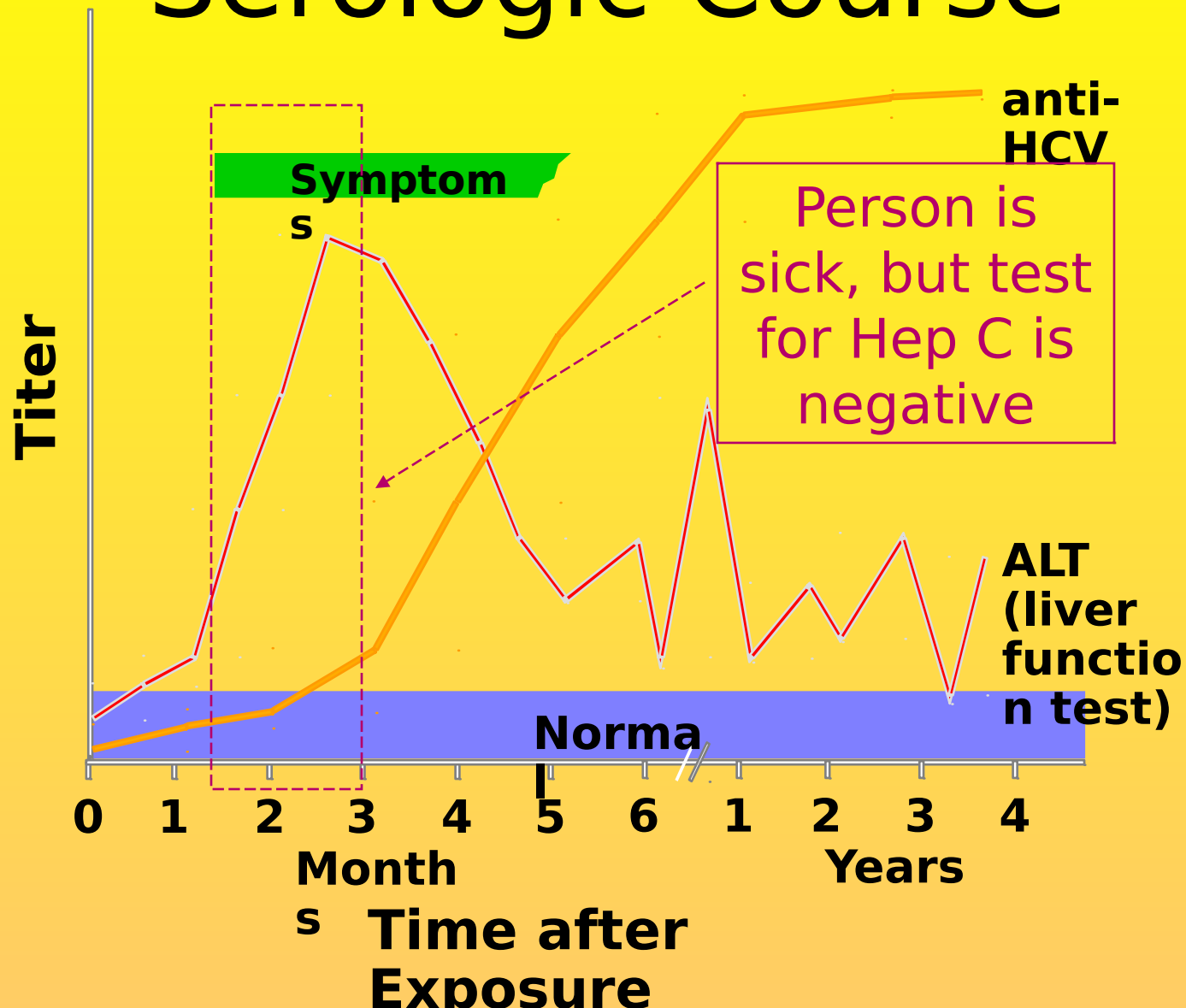
Serologic test detects HCV antibody

Positive in chronic cases

May not be positive in acute phase

Rule out other causes of acute hepatitis

Hepatitis C: Typical Serologic Course



Hepatitis C Prevention

Education

- High-risk behavior modification

- Same risk factors as hepatitis B

- Blood > sex > perinatal

- Blood and body fluid precautions

- Screening of blood, organ, tissue donors

- No vaccine, antibodies do not protect

- IG does not protect

Hepatitis C Review

Clinically similar to hepatitis B

Transmission similar to hepatitis B

Blood > sex > perinatal

Today, transfusion is low-risk

Serologic test detects antibody

May not be positive acutely

Prevention

Education only, no vaccine

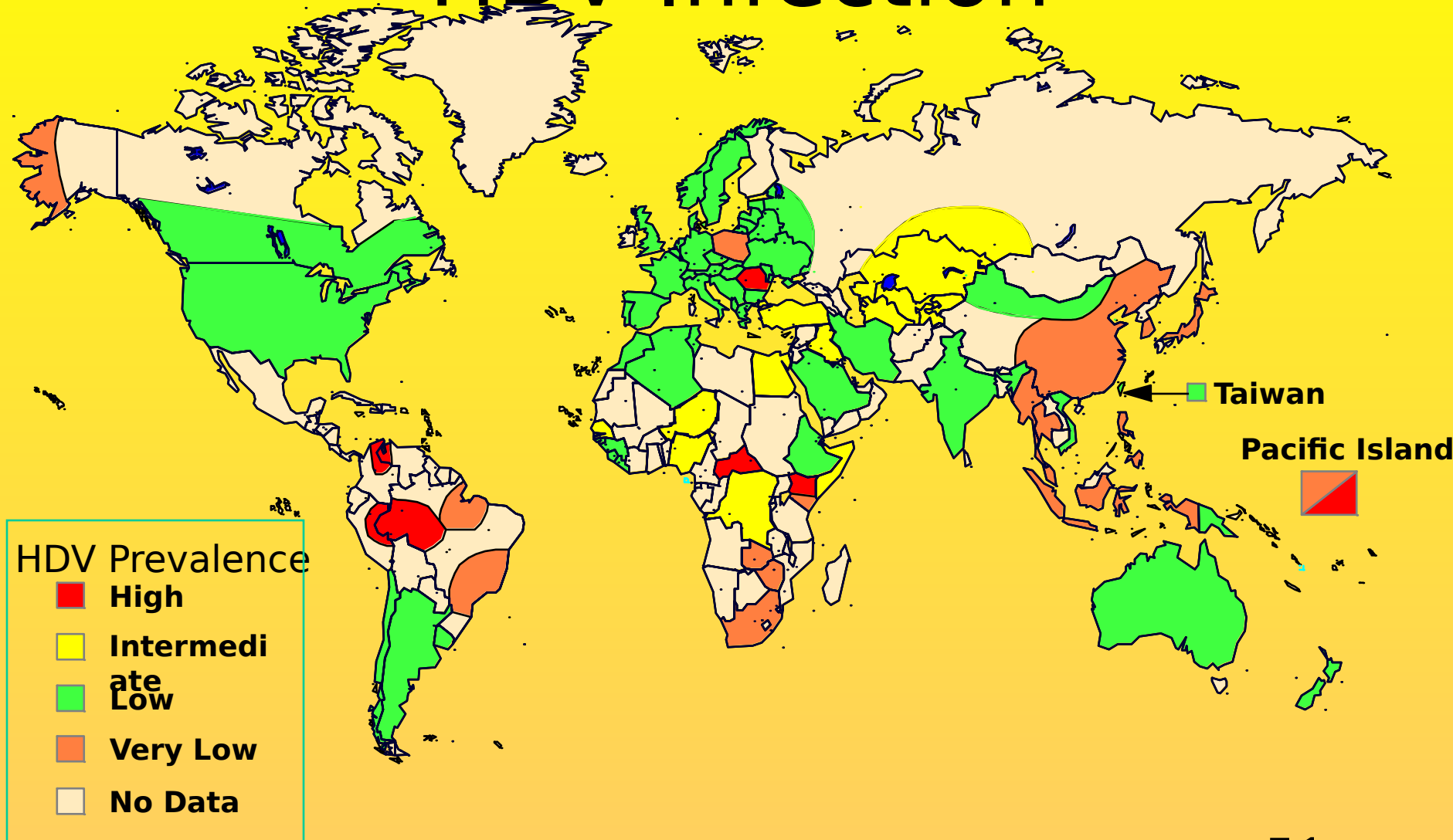
Hepatitis D

“delta hepatitis”

Caused by an incomplete RNA virus
Requires HBV co-infection to replicate

Parenteral & sexual transmission
similar to hepatitis B

Geographic Distribution of HDV Infection



Hepatitis D: Clinical Aspects

Incubation period 42-180 days

Onset abrupt or insidious

Symptoms severe

Complications

- 70% eventually develop cirrhosis

- 10-15% develop cirrhosis within two years

- 2-20% fatality rate

20-50% of fulminate liver failure in
hepatitis B

actually due to hepatitis D co-infection

Hepatitis D Diagnosis and Prevention

Diagnosis

Serologic test for hepatitis D antibody

Prevention

Hepatitis B vaccine

Anyone who is HBsAg positive
is at risk for hepatitis D

Hepatitis E

“enterically transmitted non-A, non-B hepatitis”

Caused by a non-enveloped RNA calicivirus

Transmission similar to hepatitis A

Outbreaks associated with poor sanitation

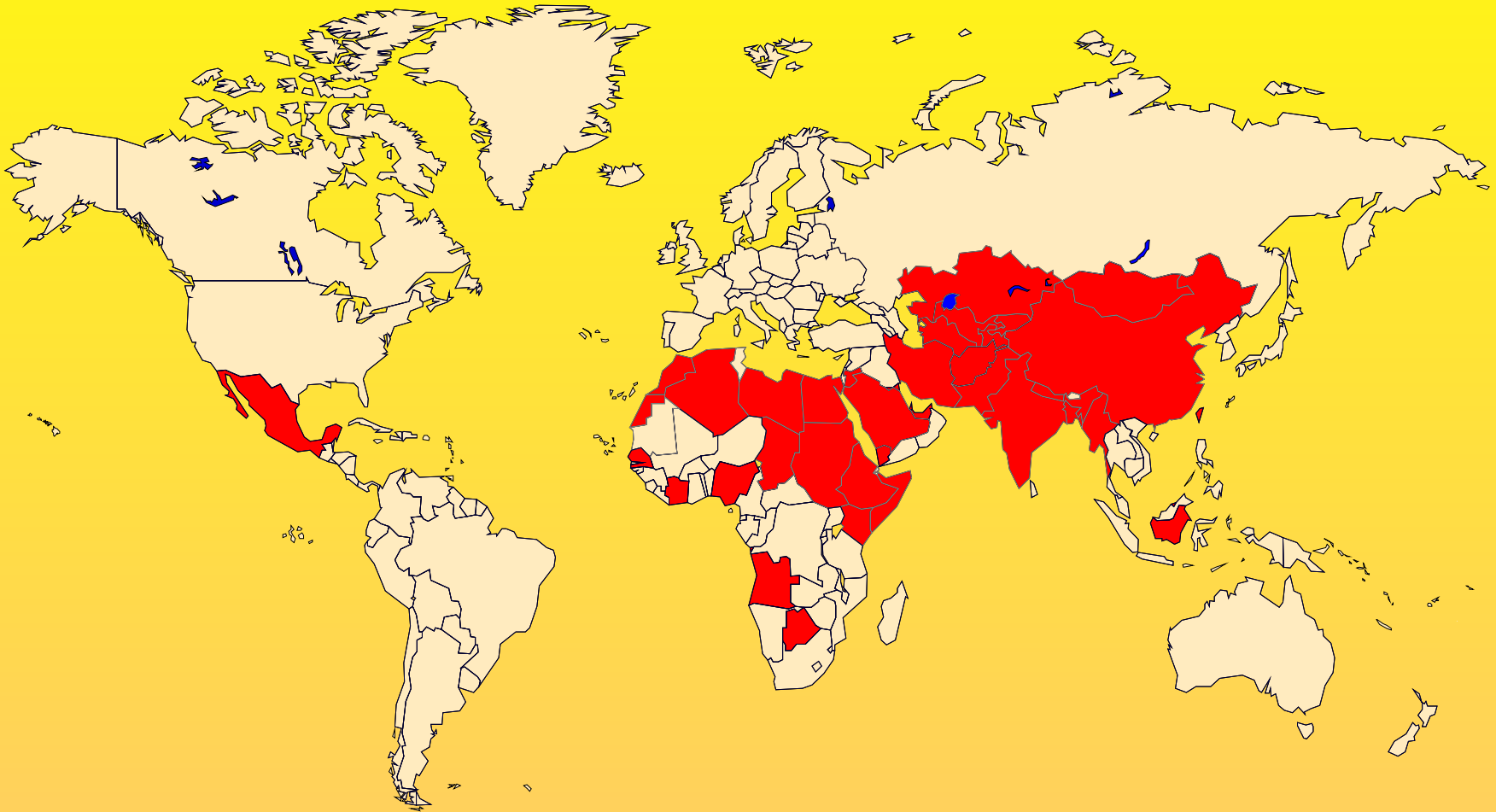
Waterborne epidemics & sporadic cases

Person to person spread uncommon

Occurs in India, central and southeast Asia, middle east, Africa, and Mexico

Almost all cases in U.S. acquired elsewhere

Geographic Distribution of Hepatitis E Outbreaks or Confirmed Infection in >25% of Sporadic Non-ABC Hepatitis



Hepatitis E: Clinical Aspects

Incubation period

15-60 days, average ± 40

Illness severity increases with age

Overall case-fatality rate: 1%-3%

Causes severe illness in pregnant with

15%-25% fatality rate

No chronic carriers

Hepatitis E Diagnosis

1. Hepatitis symptoms
2. Elevated LFTs
3. Serologic test - research use only
Evaluate risk factors, exposure history
Rule out hepatitis A (B, C, and D)

Hepatitis E Prevention

Immune globulin does not protect

Strict food & water precautions
will prevent

Avoid contaminated water

Avoid uncooked food

New Hepatitis Viruses

Are there enough letters in the
alphabet?

Hepatitis G

(non-A, non-B, non-C, non-D, non-E

RNA flavivirus hepatitis)

Distantly related to hepatitis C virus

0.3% of acute viral hepatitis

900-2000 infections/year

Bloodborne transmission

Chronic infection

PCR based laboratory diagnosis

Hepatitis G

Endemic worldwide

Recently identified

New technology

Emerging vs re-emerging

Identified in archival specimens
from 1978

Hepatitis G

- 13 cases of post-transfusion hepatitis
 - 3 patients were HGV RNA negative before transfusion and positive for HGV after
- CDC - 38 acute hepatitis pts neg for hep A-E
 - 5 (13%) positive for HGV
- CDC - 107 with acute hepatitis C
 - 19 (18%) also had HGV RNA
- 779 U.S. volunteer blood donors
 - All had normal alanine aminotransferase
 - 13 (1.3%) positive for HGV

Medical Event Reports (MERS)

Required on all cases of acute hepatitis

Must include:

1. Date
2. Reporting command
3. POC info
4. Pt name
5. SSN
6. Branch of service
7. Pt command & UIC
8. Diagnosis (incl ICD-9 code)
9. Suspected or confirmed (state clinical or laboratory confirmation)
10. Date of onset
11. Disposition
12. Comments (optional)

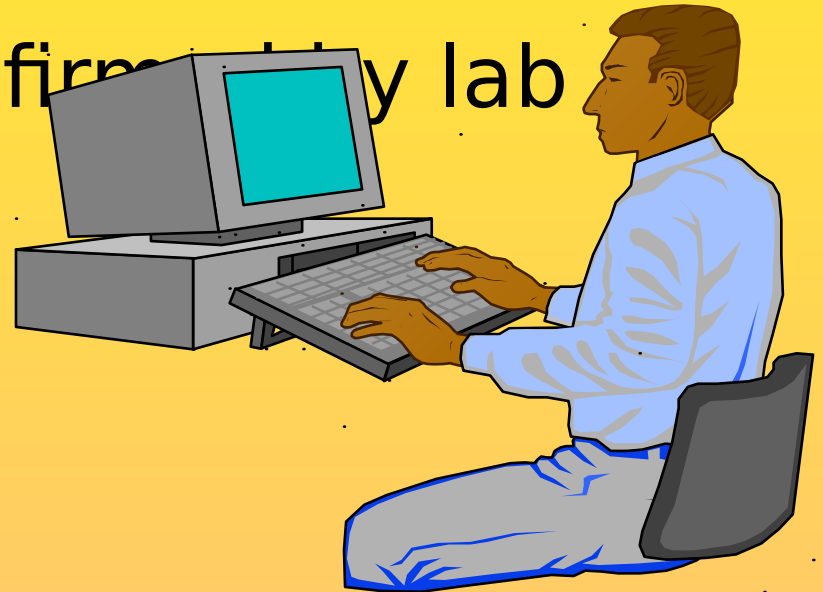
Medical Event Reports

Submit initial MER on suspected cases

Before evaluation is complete

Submit final MER

When case is confirmed by lab work



Viral Hepatitis Review

Inflammation of the liver

Caused by 5 different viruses

Similar symptoms

Different antigenic properties

Different epidemiology

- A & E spread by fecal-oral contamination

- B, C, & D are spread parenterally
(Blood, sex, perinatal)

MER required on all cases of acute hepatitis

Viral Hepatitis Prevention Review

Hepatitis A & E

Safe food and
water

Hepatitis A only

Hep A Vaccine
IG

Hepatitis B, C & D

Avoid risk related
behaviors

Hepatitis B & D

Hep B Vaccine

Hepatitis B only

HBIG

Cases for Discussion

True life adventures in Navy epidemiology and preventive medicine



Typical Case # 1

22 yo mess specialist, born in a country with high endemic rates of hepatitis

Positive for hepatitis B surface antigen

Negative for hepatitis B surface antibody

Negative for hepatitis A antibody

Normal LFTs

No symptoms

Can he work in the galley?

Typical Case # 1a

22 yo HM3, born in a highly endemic country

Positive for hepatitis B surface antigen

Negative for hepatitis B surface antibody

Negative for hepatitis A antibody

Normal LFTs

No symptoms

Can he work in the blood bank?

Typical Case # 2

32 yo CHT worker

Exposed to human sewage while repairing pipes

Does he need hepatitis B vaccine?

Does he need IG?

Does he need hepatitis A vaccine?

Should his wife get shots?

Typical Case # 3

24 yo mess specialist

Chronic fatigue for past 4 weeks

Abdominal pain about 3 or 4 weeks ago -
now resolved

LFTs normal

Positive for IgM hepatitis A antibody

Does entire crew need IG?
Can he work in the galley?

Typical Case # 4

30 yo Sailor

Abdominal pain for 2 weeks

Now has yellow eyes

LFTs elevated - 5 times normal

Positive for hepatitis B surface antibody

Negative for hepatitis B surface antigen

Negative for hepatitis A antibody

What has he got?

Typical Case # 4

More information

Negative for hepatitis C antibody

No history of unsafe sex sex in past 6 months

No history of tattoos or other needle use

No history of alcohol abuse

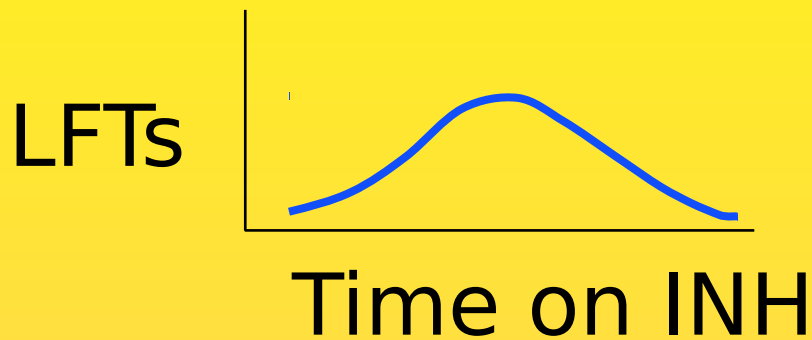
PPD convertor

Taking INH for past 2 months without problems

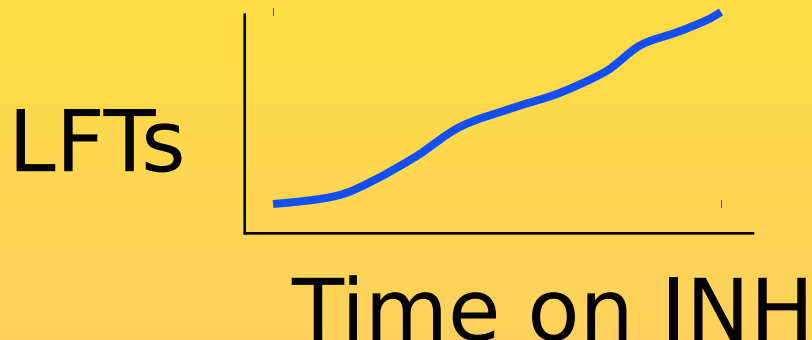
What has he got?

INH Associated Hepatitis

LFTs usually rise with INH therapy



Normal 4-fold rise
in LFTs -
returns to baseline



Greater than 4-fold
rise in LFTs -
indicates toxicity

Acute Hepatitis Treatment

- Supportive care
- Avoidance of further liver damage
 - No meds
- Isolation - prior to diagnosis
- Medical follow up
 - Check LFTs twice per week if increasing
 - Check LFTs once per week after plateau
 - Check LFTs every 1-2 weeks while declining

Questions?